

SEQUENCE LISTING

<110> Conaris Research Institute GmbH

<120> Diagnostic Use of Polymorphisms in the Gene Coding for
the TNF Receptor II and Method for Detecting
Non-Responders to Anti-TNF-Therapy

<130> K51347/8

<140>

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<170> PatentIn Ver. 2:1

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09902175.071001

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09902476-071001

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0990217E-071001

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00902476 071001

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0990217E-071001

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26

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Met Ala Pro Val Ala Val Trp Ala
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gcg ctg gcc gtc gga ctg gag ctc tgg gct gcg gcg cac gcc ttg ccc 161
Ala Leu Ala Val Gly Leu Glu Leu Trp Ala Ala Ala His Ala Leu Pro
-10 -5 -1 1

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Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys
5 10 15

cgg ctc aga gaa tac tat gac cag aca gct cag atg tgc tgc agc aaa 257
Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys
20 25 30

tgc tcg ccg ggc caa cat gca aaa gtc ttc tgt acc aag acc tcg gac	305
Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp	
35 40 45 50	
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Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn	
55 60 65	
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Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln	
70 75 80	
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Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr Cys	
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agg ccc ggc tgg tac tgc gcg ctg agc aag cag gag ggg tgc cgg ctg	497
Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu	
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Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro	
115 120 125 130	
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Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr	
135 140 145	
ttc tcc aac acg act tca tcc acg gat att tgc agg ccc cac cag atc	641
Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His Gln Ile	
150 155 160	
tgt aac gtg gtg gcc atc cct ggg aat gca agc atg gat gca gtc tgc	689
Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala Val Cys	
165 170 175	
acg tcc acg tcc ccc acc cgg agt atg gcc cca ggg gca gta cac tta	737
Thr Ser Thr Ser Pro Thr Arg Ser Met Ala Pro Gly Ala Val His Leu	
180 185 190	
ccc cag cca gtg tcc aca cga tcc caa cac acg cag cca act cca gaa	785
Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr Pro Glu	
195 200 205 210	
ccc agc act gct cca agc acc tcc ttc ctg ctc cca atg ggc ccc agc	833
Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro Met Gly Pro Ser	
215 220 225	

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Pro Pro Ala Glu Gly Ser Thr Gly Asp Phe Ala Leu Pro Val Gly Leu	
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att gtg ggt gtg aca gcc ttg ggt cta cta ata ata gga gtg gtg aac	929
Ile Val Gly Val Thr Ala Leu Gly Leu Leu Ile Ile Gly Val Val Asn	
245 250 255	
tgt gtc atc atg acc cag gtg aaa aag aag ccc ttg tgc ctg cag aga	977
Cys Val Ile Met Thr Gln Val Lys Lys Lys Pro Leu Cys Leu Gln Arg	
260 265 270	
gaa gcc aag gtg cct cac ttg cct gcc gat aag gcc cgg ggt aca cag	1025
Glu Ala Lys Val Pro His Leu Pro Ala Asp Lys Ala Arg Gly Thr Gln	
275 280 285 290	
ggc ccc gag cag cag cac ctg ctg atc aca gcg ccg agc tcc agc agc	1073
Gly Pro Glu Gln Gln His Leu Leu Ile Thr Ala Pro Ser Ser Ser Ser	
295 300 305	
agc tcc ctg gag agc tcg gcc agt gcg ttg gac aga agg gcg ccc act	1121
Ser Ser Leu Glu Ser Ser Ala Ser Ala Leu Asp Arg Arg Ala Pro Thr	
310 315 320	
cgg aac cag cca cag gca cca ggc gtg gag gcc agt ggg gcc ggg gag	1169
Arg Asn Gln Pro Gln Ala Pro Gly Val Glu Ala Ser Gly Ala Gly Glu	
325 330 335	
gcc cgg gcc agc acc ggg agc tca gat tct tcc cct ggt ggc cat ggg	1217
Ala Arg Ala Ser Thr Gly Ser Ser Asp Ser Ser Pro Gly Gly His Gly	
340 345 350	
acc cag gtc aat gtc acc tgc atc gtg aac gtc tgt agc agc tct gac	1265
Thr Gln Val Asn Val Thr Cys Ile Val Asn Val Cys Ser Ser Ser Asp	
355 360 365 370	
cac agc tca cag tgc tcc tcc caa gcc agc tcc aca atg gga gac aca	1313
His Ser Ser Gln Cys Ser Ser Gln Ala Ser Ser Thr Met Gly Asp Thr	
375 380 385	
gat tcc agc ccc tcg gag tcc ccg aag gac gag cag gtc ccc ttc tcc	1361
Asp Ser Ser Pro Ser Glu Ser Pro Lys Asp Glu Gln Val Pro Phe Ser	
390 395 400	
aag gag gaa tgt gcc ttt cgg tca cag ctg gag acg cca gag acc ctg	1409
Lys Glu Glu Cys Ala Phe Arg Ser Gln Leu Glu Thr Pro Glu Thr Leu	
405 410 415	

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 Leu Gly Ser Thr Glu Glu Lys Pro Leu Pro Leu Gly Val Pro Asp Ala
 420 425 430

ggg atg aag ccc agt taa ccaggccggt gtgggctgtg tcgtagccaa 1505
 Gly Met Lys Pro Ser
 435 440

ggtgggctga gccctggcag gatgaccctg cgaagggggcc ctggtccttc caggccccca 1565

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aacccccac ctgccatttg caccctccgc cttcactccg gtgtgcctgc agccccgcgc 2645

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09902176 071001

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35 40 45

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Ser	Thr	Tyr	Thr	Gln	Leu	Trp	Asn	Trp	Val	Pro	Glu	Cys	Leu	Ser	Cys
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Gly	Ser	Arg	Cys	Ser	Ser	Asp	Gln	Val	Glu	Thr	Gln	Ala	Cys	Thr	Arg
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Glu	Gln	Asn	Arg	Ile	Cys	Thr	Cys	Arg	Pro	Gly	Trp	Tyr	Cys	Ala	Leu
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Pro	Gly	Phe	Gly	Val	Ala	Arg	Pro	Gly	Thr	Glu	Thr	Ser	Asp	Val	Val
145					150					155					160
Cys	Lys	Pro	Cys	Ala	Pro	Gly	Thr	Phe	Ser	Asn	Thr	Thr	Ser	Ser	Thr
				165					170						175
Asp	Ile	Cys	Arg	Pro	His	Gln	Ile	Cys	Asn	Val	Val	Ala	Ile	Pro	Gly
			180					185						190	
Asn	Ala	Ser	Met	Asp	Ala	Val	Cys	Thr	Ser	Thr	Ser	Pro	Thr	Arg	Ser
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225					230					235					240
Phe	Leu	Leu	Pro	Met	Gly	Pro	Ser	Pro	Pro	Ala	Glu	Gly	Ser	Thr	Gly
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Asp	Phe	Ala	Leu	Pro	Val	Gly	Leu	Ile	Val	Gly	Val	Thr	Ala	Leu	Gly
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Leu	Leu	Ile	Ile	Gly	Val	Val	Asn	Cys	Val	Ile	Met	Thr	Gln	Val	Lys
		275					280					285			
Lys	Lys	Pro	Leu	Cys	Leu	Gln	Arg	Glu	Ala	Lys	Val	Pro	His	Leu	Pro
	290					295					300				
Ala	Asp	Lys	Ala	Arg	Gly	Thr	Gln	Gly	Pro	Glu	Gln	Gln	His	Leu	Leu
305					310					315					320
Ile	Thr	Ala	Pro	Ser	Ser	Ser	Ser	Ser	Ser	Leu	Glu	Ser	Ser	Ala	Ser
				325					330						335
Ala	Leu	Asp	Arg	Arg	Ala	Pro	Thr	Arg	Asn	Gln	Pro	Gln	Ala	Pro	Gly
			340					345						350	
Val	Glu	Ala	Ser	Gly	Ala	Gly	Glu	Ala	Arg	Ala	Ser	Thr	Gly	Ser	Ser
		355					360					365			
Asp	Ser	Ser	Pro	Gly	Gly	His	Gly	Thr	Gln	Val	Asn	Val	Thr	Cys	Ile
	370					375					380				
Val	Asn	Val	Cys	Ser	Ser	Ser	Asp	His	Ser	Ser	Gln	Cys	Ser	Ser	Gln
385					390						395				400
Ala	Ser	Ser	Thr	Met	Gly	Asp	Thr	Asp	Ser	Ser	Pro	Ser	Glu	Ser	Pro
				405					410						415
Lys	Asp	Glu	Gln	Val	Pro	Phe	Ser	Lys	Glu	Glu	Cys	Ala	Phe	Arg	Ser
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 Met Ala Pro Val Ala Val Trp Ala
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 Ala Leu Ala Val Gly Leu Glu Leu Trp Ala Ala Ala His Ala Leu Pro
 -10 -5 -1 1
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 Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys
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 Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys
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 tgc tcg ccg ggc caa cat gca aaa gtc ttc tgt acc aag acc tcg gac 305
 Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp
 35 40 45 50
 acc gtg tgt gac tcc tgt gag gac agc aca tac acc cag ctc tgg aac 353
 Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn
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Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln
70 75 80

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Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr Cys
85 90 95

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Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu
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Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro
115 120 125 130

gga act gaa aca tca gac gtg gtg tgc aag ccc tgt gcc ccg ggg acg 593
Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr
135 140 145

ttc tcc aac acg act tca tcc acg gat att tgc agg ccc cac cag atc 641
Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His Gln Ile
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tgt aac gtg gtg gcc atc cct ggg aat gca agc atg gat gca gtc tgc 689
Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala Val Cys
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Thr Ser Thr Ser Pro Thr Arg Ser Met Ala Pro Gly Ala Val His Leu
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Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr Pro Glu
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ccc agc act gct cca agc acc tcc ttc ctg ctc cca atg ggc ccc agc 833
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Pro Pro Ala Glu Gly Ser Thr Gly Asp Phe Ala Leu Pro Val Gly Leu
230 235 240

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Ile Val Gly Val Thr Ala Leu Gly Leu Leu Ile Ile Gly Val Val Asn
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tgt gtc atc atg acc cag gtg aaa aag aag ccc ttg tgc ctg cag aga 977

09902175-071001

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 Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys
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 Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp
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 85 90 95
 Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
 100 105 110
 Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu
 115 120 125

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Pro	Gly	Phe	Gly	Val	Ala	Arg	Pro	Gly	Thr	Glu	Thr	Ser	Asp	Val	Val	145	150	155
Cys	Lys	Pro	Cys	Ala	Pro	Gly	Thr	Phe	Ser	Asn	Thr	Thr	Ser	Ser	Thr	165	170	175
Asp	Ile	Cys	Arg	Pro	His	Gln	Ile	Cys	Asn	Val	Val	Ala	Ile	Pro	Gly	180	185	190
Asn	Ala	Ser	Met	Asp	Ala	Val	Cys	Thr	Ser	Thr	Ser	Pro	Thr	Arg	Ser	195	200	205
Met	Ala	Pro	Gly	Ala	Val	His	Leu	Pro	Gln	Pro	Val	Ser	Thr	Arg	Ser	210	215	220
Gln	His	Thr	Gln	Pro	Thr	Pro	Glu	Pro	Ser	Thr	Ala	Pro	Ser	Thr	Ser	225	230	235
Phe	Leu	Leu	Pro	Met	Gly	Pro	Ser	Pro	Pro	Ala	Glu	Gly	Ser	Thr	Gly	245	250	255
Asp	Phe	Ala	Leu	Pro	Val	Gly	Leu	Ile	Val	Gly	Val	Thr	Ala	Leu	Gly	260	265	270
Leu	Leu	Ile	Ile	Gly	Val	Val	Asn	Cys	Val	Ile	Met	Thr	Gln	Val	Lys	275	280	285
Lys	Lys	Pro	Leu	Cys	Leu	Gln	Arg	Glu	Ala	Lys	Val	Pro	His	Leu	Pro	290	295	300
Ala	Asp	Lys	Ala	Arg	Gly	Thr	Gln	Gly	Pro	Glu	Gln	Gln	His	Leu	Leu	305	310	315
Ile	Thr	Ala	Pro	Ser	Ser	Ser	Ser	Ser	Ser	Ser	Leu	Glu	Ser	Ser	Ala	325	330	335
Ala	Leu	Asp	Arg	Arg	Ala	Pro	Thr	Arg	Asn	Gln	Pro	Gln	Ala	Pro	Gly	340	345	350
Val	Glu	Ala	Ser	Gly	Ala	Gly	Glu	Ala	Arg	Ala	Ser	Thr	Gly	Ser	Ser	355	360	365
Asp	Ser	Ser	Pro	Gly	Gly	His	Gly	Thr	Gln	Val	Asn	Val	Thr	Cys	Ile	370	375	380
Val	Asn	Val	Cys	Ser	Ser	Ser	Asp	His	Ser	Ser	Gln	Cys	Ser	Ser	Gln	385	390	395
Ala	Ser	Ser	Thr	Met	Gly	Asp	Thr	Asp	Ser	Ser	Pro	Ser	Glu	Ser	Pro	405	410	415
Lys	Asp	Glu	Gln	Val	Pro	Phe	Ser	Lys	Glu	Glu	Cys	Ala	Phe	Arg	Ser	420	425	430
Gln	Leu	Glu	Thr	Pro	Glu	Thr	Leu	Leu	Gly	Ser	Thr	Glu	Glu	Lys	Pro	435	440	445
Leu	Pro	Leu	Gly	Val	Pro	Asp	Ala	Gly	Met	Lys	Pro	Ser				450	455	460

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<213> Homo sapiens

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Met Ala Pro Val Ala Val Trp Ala
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gcg ctg gcc gtc gga ctg gag ctc tgg gct gcg gcg cac gcc ttg ccc 161
Ala Leu Ala Val Gly Leu Glu Leu Trp Ala Ala Ala His Ala Leu Pro
-10 -5 -1 1

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Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys
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Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys
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tgc tcg ccg ggc caa cat gca aaa gtc ttc tgt acc aag acc tcg gac 305
Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp
35 40 45 50

acc gtg tgt gac tcc tgt gag gac agc aca tac acc cag ctc tgg aac 353
Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn
55 60 65

tgg gtt ccc gag tgc ttg agc tgt ggc tcc cgc tgt agc tct gac cag 401
Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln
70 75 80

gtg gaa act caa gcc tgc act cgg gaa cag aac cgc atc tgc acc tgc 449
Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr Cys
85 90 95

agg ccc ggc tgg tac tgc gcg ctg agc aag cag gag ggg tgc cgg ctg 497
Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu
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 Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro
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gga act gaa aca tca gac gtg gtg tgc aag ccc tgt gcc ccg ggg acg 593
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 Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Arg Asp Ala Val Cys
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acg tcc acg tcc ccc acc cgg agt atg gcc cca ggg gca gta cac tta 737
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 Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr Pro Glu
 195 200 205 210

ccc agc act gct cca agc acc tcc ttc ctg ctc cca atg ggc ccc agc 833
 Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro Met Gly Pro Ser
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 Gly Met Lys Pro Ser
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 35 40 45
 Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys
 50 55 60
 Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp
 65 70 75 80
 Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys
 85 90 95
 Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
 100 105 110
 Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu
 115 120 125
 Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg
 130 135 140
 Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val
 145 150 155 160
 Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr
 165 170 175
 Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly
 180 185 190
 Asn Ala Ser Arg Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser
 195 200 205

Met	Ala	Pro	Gly	Ala	Val	His	Leu	Pro	Gln	Pro	Val	Ser	Thr	Arg	Ser	210	215	220
Gln	His	Thr	Gln	Pro	Thr	Pro	Glu	Pro	Ser	Thr	Ala	Pro	Ser	Thr	Ser	225	230	235
Phe	Leu	Leu	Pro	Met	Gly	Pro	Ser	Pro	Pro	Ala	Glu	Gly	Ser	Thr	Gly	245	250	255
Asp	Phe	Ala	Leu	Pro	Val	Gly	Leu	Ile	Val	Gly	Val	Thr	Ala	Leu	Gly	260	265	270
Leu	Leu	Ile	Ile	Gly	Val	Val	Asn	Cys	Val	Ile	Met	Thr	Gln	Val	Lys	275	280	285
Lys	Lys	Pro	Leu	Cys	Leu	Gln	Arg	Glu	Ala	Lys	Val	Pro	His	Leu	Pro	290	295	300
Ala	Asp	Lys	Ala	Arg	Gly	Thr	Gln	Gly	Pro	Glu	Gln	Gln	His	Leu	Leu	305	310	315
Ile	Thr	Ala	Pro	Ser	Ser	Ser	Ser	Ser	Ser	Leu	Glu	Ser	Ser	Ala	Ser	325	330	335
Ala	Leu	Asp	Arg	Arg	Ala	Pro	Thr	Arg	Asn	Gln	Pro	Gln	Ala	Pro	Gly	340	345	350
Val	Glu	Ala	Ser	Gly	Ala	Gly	Glu	Ala	Arg	Ala	Ser	Thr	Gly	Ser	Ser	355	360	365
Asp	Ser	Ser	Pro	Gly	Gly	His	Gly	Thr	Gln	Val	Asn	Val	Thr	Cys	Ile	370	375	380
Val	Asn	Val	Cys	Ser	Ser	Ser	Asp	His	Ser	Ser	Gln	Cys	Ser	Ser	Gln	385	390	395
Ala	Ser	Ser	Thr	Met	Gly	Asp	Thr	Asp	Ser	Ser	Pro	Ser	Glu	Ser	Pro	405	410	415
Lys	Asp	Glu	Gln	Val	Pro	Phe	Ser	Lys	Glu	Glu	Cys	Ala	Phe	Arg	Ser	420	425	430
Gln	Leu	Glu	Thr	Pro	Glu	Thr	Leu	Leu	Gly	Ser	Thr	Glu	Glu	Lys	Pro	435	440	445
Leu	Pro	Leu	Gly	Val	Pro	Asp	Ala	Gly	Met	Lys	Pro	Ser				450	455	460